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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/516,744

12/06/2004

Eric Trinquet

LOM-0042

6942

23599 7590 10/16/2008
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EXAMINER

STAPLES, MARK

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

10/16/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/516,744	Applicant(s) TRINQUET ET AL.	
	Examiner Mark Staples	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09/23/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-44, 47-58, 60, 63, 65 and 66 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-44, 47-58, 60, 63, 65 and 66 is/are rejected.
- 7) ☒ Claim(s) 60, 65, and 66 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/23/2008 has been entered.

2. Applicant's amendment of claims 42-44, 47-58, and 60, the cancellation of claims 45, 46, 59, 61, 62, and 64, and submission of new claim 65 and 66 in the paper filed on 08/22/2008 is acknowledged.

Claims 42-44, 47-58, 60, 63, 65, and 66 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections that are Moot / Withdrawn

Canceled Claim Objections and Rejections Moot / Withdrawn

3. The objections and rejections of canceled claims 45, 46, 59, 61, 62, and 64, are moot and therefore are withdrawn.

Sequence Rules Compliance Moot

4. The objection to canceled claim 61 for not complying with sequence rules is moot and therefore is withdrawn.

Claim Rejections Withdrawn - 35 USC § 102(b)

5. The rejection of claims 42-44, 46, 47, 51-56, 59-61, 64, and 64 under 35 U.S.C. 102(b) as being anticipated by Tyagi et al. (1999) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

Claim Rejections Withdrawn - 35 USC § 103(a)

6. The rejection of claims 45, 48, 57, and 62 under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. further in view of Glazer et al. (1998) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

7. The rejection of 49 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. and Glazer et al. further in view of Surrey et al. (1964) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

New Objections and Rejections Necessitated by Amendment

New Claim Objections

8. Claim 60 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Antecedent claim 42 already recites wherein the carrier molecule is an antibody and thus dependent claim 60 is not further limiting.

9. Claim 65 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Antecedent claim 42 already recites wherein the carrier molecule is an antibody and thus dependent claim 65 is not further limiting as neither strepavidin nor avidin is an antibody.

10. Claim 66 is objected to for improper use of the trademark CY5™. It and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to scan the entire application to ensure trademark usage in all the places where it appears in the application is in compliance with the current office guidelines.

New Claim Rejections - 35 USC § 112

11. Claim 66 contains the trademark/trade name CY5™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the cyanine and, accordingly, the identification/description is indefinite.

New Claim Rejections - 35 USC § 103(a)

12. Claims 42-44, 47, 49-58, 60, 63, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Langel et al. (United States Patent 6,025,140 issued 2000) and Walker et al. (1995).

Regarding claims 42, 47, 52, 55, 60, Langel et al. a labeled conjugate which is a cyanine oligonucleotide-peptide conjugate (entire patent) comprising:

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- a cyanine dye covalently attached to an oligonucleotide (see claim 10 and column 7 lines 46-53),

- a carrier molecule which is an peptide (see claim 1 and see Figure 5) and by incorporation of reference to Walker et al. (see list of references and see column 24 lines 1-4) further suggest that the carrier molecule can be an antibody (see title of the reference of Walker et al.),

said entity being covalently attached to said carrier molecule by means of at least one functional group on the oligonucleotide (see Scheme 1), said functional group which can be an amino group of a modified nucleobase in the oligonucleotide (see column 13 lines 52-63).

Regarding claim 42, Langel et al. teach cyanine labeled oligonucleotide-peptide conjugates, reference oligonucleotide-antibody conjugates and suggest these but do not specifically teach a cyanine labeled oligonucleotide-antibody conjugates.

Regarding claims 43, 50, and 63, Langel et al. teach an oligonucleotide which is 15 nucleotide units (see Figure 3).

Regarding claim 44, Langel et al. teach linkers/spacer arms (see column 9 lines 4-6 and see Figure 3).

Regarding claim 51, Langel et al. teach the DNA or RNA units are attached through phosphodiester bonds (see column 8 lines 21-37).

Regarding claim 53, Langel et al. teach PNA analog nucleoside units attached to each other by amide bonds (see column 11 line 65 to column 12 line 6).

Regarding claims 54 and 56, Langel et al. teach PNA analog nucleoside units attached to each other by amide bonds (see column 11 line 65 to column 12 line 6) and teach at least 5 internucleotide phosphodiester bonds at the end intended to be attached to the fluorophore (see column 8 lines 21-37 and see Figure 3).

Regarding claim 65, Langel et al. teach streptavidin (see Example 5).

Regarding claim 42, Walker et al. a labeled conjugate which is a radiolabeled oligonucleotide-antibody conjugate (entire article, especially Scheme 1) comprising:

- a radiolabel covalently attached to the 3' end of an oligonucleotide (see legend to Figure 1)
- a carrier molecule which is an antibody (see Scheme 1)

said entity being covalently attached to said carrier molecule by means of at least one functional group on the oligonucleotide (see Scheme 1), said functional group being an maleimide group (again see Scheme 1).

Regarding claim 42, Walker et al. teach a label but do not specifically teach a fluorescent label and do not specifically teach a cyanine dye.

Regarding claim 49, 57, and 58, Walker et al. teach a spacer arm of the first listed formula (see Scheme 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the cyanine labeled oligonucleotide-peptide conjugate of Langel et al. by substituting an antibody for the peptide as

suggested by Walker et al. with a reasonable expectation of success. The motivation to do so is provided by Langel et al. who teach that the reference of Walker et al. is specifically and individually incorporated by reference (see column 24 lines 1-4). Further motivation to do so is provided by Walker et al. who teach that oligonucleotide-antibody conjugates improve cellular delivery of therapeutic antisense oligonucleotides (see 1st sentence on p. 1548 and see 2nd paragraph on p. 1552). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

13. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Langel et al. and Walker et al. as applied to claim 47 above, and further in view of Glazer et al. (1998, previously cited).

Langel et al. and Walker et al. teach noted above.

Langel et al. and Walker et al. teach spacer arms but do not specifically teach an alkylene spacer arm.

Regarding claim 48, Glazer et al. teach a linear alkylene spacer arm having a divalent organic radical which can be of the length of C₁-C₂₀ and containing one hetero atom, N (see the structure at column 8, lines 14-22 and see claim 27). Glazer et al. also teach where the fluorophore which cyanine (see Title and Abstract).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the spacer arm of Langel et al. and Walker et al. by substituting a linear alkylene spacer arm having a divalent organic radical as suggested by Glazer et al. with a reasonable expectation of success. The

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motivation to do so is provided by Glazer et al. who teach the 20 atom length specifically for use with oligonucleotides: "Linkage of the fluorophores to the backbone is achieved by conventional covalent binding. . . .In the case of nucleic acid backbones [oligonucleotides], linkage is preferably achieved by use of a convenient linking arm usually consisting of from about 2 to about 20 . . . atoms" (see column 7 line 65 through to column 8 line 9). Glazer et al. further teach: "A preferred linking group structure is an amide-containing chain . . . (see column 8 lines 10-111). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

14. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Langel et al. and Walker et al. as applied to claim 47 above, and further in view of Zuk et al. (United States Patent 5,650,334 issued 1997).

Langel et al. and Walker et al. teach noted above.

Langel et al. and Walker et al. teach cyanine dyes but do not specifically teach the cyanine dye which is CY5™.

Regarding claim 66, Zuk et al. teach labeling nucleic acids with CY5™, an arylsulfonate cyanine dye. (see Abstract and see claim 10).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the cyanine dye of Langel et al. and Walker et al. by substituting CY5™, an arylsulfonate cyanine dye, as suggested by Zuk et al. with a reasonable expectation of success. The motivation to do so is provided by Zuk et al. who teach that labeling with CY5™, an arylsulfonate cyanine dye, provides:

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“ . . . substantially enhanced fluorescent emission levels (signal amplification) with reduced self-quenching” (see column 3 lines 34-36) . Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

15. No claim is free of the prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Mark Staples

/M.S./

Examiner, Art Unit 1637

October 8, 2008

/Kenneth R Horlick/

Primary Examiner, Art Unit 1637